

Appl. No. : **09/787,356**
Filed : **June 25, 2001**

AMENDMENTS TO THE CLAIMS

1. (Previously Presented) A method for mediating relaxation of an airway of an animal, said method comprising administering to said animal, an amount of a peptide effective for mediating relaxation of said airway, said peptide having a sequence comprising SLIGRL (SEQ ID NO:2) or a peptide analog thereof in which an amino acid is replaced with a non-natural amino acid, wherein said peptide is capable of activating an airway epithelium protease activated receptor-2 (PAR2) under conditions sufficient for activation of said PAR2 to occur, thereby mediating relaxation of said airway.

2. (Cancelled)

3. (Cancelled)

4. (Cancelled)

5. (Previously Presented) The method according to Claim 1 wherein the relaxation of the airway is caused by a disease condition selected from the group consisting of asthma, bronchitis, hayfever, alveolitis, ciliary dyskinesis and pulmonary inflammation.

6. (Previously presented)The method according to Claim 1 wherein the peptide comprises the sequence of SEQ ID NO.2.

7. (Previously presented)The method according to Claim 6 wherein the peptide is modified to permit entry across an epithelial and/or subcutaneous layer.

8. (Previously presented)The method according to Claim 7 wherein the peptide is fused to penetratin.

9. (Previously presented)The method according to Claim 7 wherein the peptide is fused to TAT.

Claims 10-19 (Cancelled)

20. (Previously Presented) A method of identifying an agent for treatment or prophylaxis of inflammation of an airway of an animal, comprising:

exposing PAR2 to the agent; and

measuring the ability of the agent to activate the PAR2, wherein the agent is identified as capable of being useful for said treatment or prophylaxis of inflammation of an airway of an animal if it does have the ability to activate PAR2; and

further testing the peptide for treatment or prophylaxis of inflammation of an airway of an animal if it is identified as being useful.

21. (Previously presented) The method of Claim 1, wherein said peptide incorporates a non-natural amino acid.

22. (Previously presented) The method of Claim 1, wherein said peptide incorporates a non-natural amino acid listed in the following table:

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|---|-------|-----------------------------|-------|
| α -aminobutyric acid | Abu | L-N-methylalanine | Nmala |
| α -amino- α -methylbutyrate | Mgabu | L-N-methylarginine | Nmarg |
| aminocyclopropane- | Cpro | L-N-methyleasparagine | Nmasn |
| carboxylate | | L-N-methyleaspartic acid | Nmasp |
| aminoisobutyric acid | Aib | L-N-methylcysteine | Nmcys |
| aminonorbornyl- | Norb | L-N-methylglutamine | Nmgln |
| carboxylate | | L-N-methylglutamic acid | Nmglu |
| cyclohexylalanine | Chexa | L-N-methylhistidine | Nmhis |
| cyclopentylalanine | Cpen | L-N-methylisoleucine | Nmile |
| D-alanine | Dal | L-N-methylleucine | Nmleu |
| D-arginine | Darg | L-N-methyllysine | Nmlys |
| D-aspartic acid | Dasp | L-N-methylmethionine | Nmmet |
| D-cysteine | Dcys | L-N-methylnorleucine | Nmnle |
| D-glutamine | Dgln | L-N-methyinorvaline | Nmnva |
| D-glutamic acid | Dglu | L-N-methylornithine | Nmorn |
| D-histidine | Dhis | L-N-methylphenylalanine | Nmphe |
| D-isoleucine | Dile | L-N-methylproline | Nmpro |
| D-leucine | Dleu | L-N-methylserine | Nmser |
| D-lysine | Dlys | L-N-methylthreonine | Nmthr |
| D-methionine | Dmet | L-N-methyltryptophan | Nmtrp |
| D-ornithine | Dorn | L-N-methyltyrosine | Nmtyr |
| D-phenylalanine | Dphe | L-N-methylvaline | Nmval |
| D-proline | Dpro | L-N-methylethylglycine | Nmetg |

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|----------------------------------|--------|---|--------|
| D-serine | Dser | L-N-methyl-t-butylglycine | Nmtbug |
| D-threonine | Dthr | L-norleucine | Nle |
| D-tryptophan | Dtrp | L-norvaline | Nva |
| D-tyrosine | Dtyr | α -methyl-aminoisobutyrate | Maib |
| D-valine | Dval | α -methyl- γ -aminobutyrate | Mgabu |
| D- α -methylalanine | Dmala | α -methylcyclohexylalanine | Mchexa |
| D- α -methylarginine | Dmarg | α -methylcyclopentylalanine | Mcpen |
| D- α -methylasparagine | Dmasn | α -methyl- α -naphthylalanine | Manap |
| D- α -methylaspartate | Dmasp | α -methylpenicillamine | Mpen |
| D- α -methylcysteine | Dmcys | N-(4-aminobutyl)glycine | Nglu |
| D- α -methylglutamine | Dmgln | N-(2-aminoethyl)glycine | Naeg |
| D- α -methylhistidine | Dmhis | N-(3-aminopropyl)glycine | Norn |
| D- α -methylisoleucine | Dmile | N-amino- α -methylbutyrate | Nmaabu |
| D- α -methylleucine | Dmleu | α -naphthylalanine | Anap |
| D- α -methyllysine | Dmlys | N-benzylglycine | Nphe |
| D- α -methylmethionine | Dmmet | N-(2-carbamylethyl)glycine | Ngln |
| D- α -methylornithine | Dmorn | N-(carbamylmethyl)glycine | Nasn |
| D- α -methylphenylalanine | Dmphe | N-(2-carboxyethyl)glycine | Nglu |
| D- α -methylproline | Dmpro | N-(carboxymethyl)glycine | Nasp |
| D- α -methylserine | Dmser | N-cyclobutylglycine | Ncbut |
| D- α -methylthreonine | Dmthr | N-cycloheptylglycine | Nchep |
| D- α -methyltryptophan | Dmtrp | N-cyclohexylglycine | Nchex |
| D- α -methyltyrosine | Dmty | N-cyclodecylglycine | Ncdec |
| D- α -methylvaline | Dmval | N-cyclododecylglycine | Ncdod |
| D-N-methylalanine | Dnmala | N-cyclooctylglycine | Ncoct |
| D-N-methylarginine | Dnmarg | N-cyclopropylglycine | Ncpro |
| D-N-methylasparagine | Dnmasn | N-cycloundecylglycine | Ncund |
| D-N-methylaspartate | Dnmasp | N-(2,2-diphenylethyl)glycine | Nbhm |

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|-------------------------------|---------|--------------------------------------|--------|
| D-N-methylcysteine | Dnmcys | N-(3,3-diphenylpropyl)glycine | Nbhe |
| D-N-methylglutamine | Dnmgln | N-(3-guanidinopropyl)glycine | Narg |
| D-N-methylglutamate | Dnmglu | N-(1-hydroxyethyl)glycine | Nthr |
| D-N-methylhistidine | Dnmhis | N-(hydroxyethyl)glycine | Nser |
| D-N-methylisoleucine | Dnmile | N-(imidazolylethyl)glycine | Nhis |
| D-N-methylleucine | Dnmleu | N-(3-indolyethyl)glycine | Nhtrp |
| D-N-methyllysine | Dnmlys | N-methyl- γ -aminobutyrate | Nmgabu |
| N-methylcyclohexylalanine | Nmchexa | D-N-methylmethionine | Dnmmet |
| D-N-methylornithine | Dnmorn | N-methylcyclopentylalanine | Nmcpen |
| N-methylglycine | Nala | D-N-methylphenylalanine | Dnmphe |
| N-methylaminoisobutyrate | Nmaib | D-N-methylproline | Dnmpro |
| N-(1-methylpropyl)glycine | Nile | D-N-methylserine | Dnmser |
| N-(2-methylpropyl)glycine | Nleu | D-N-methylthreonine | Dnmthr |
| D-N-methyltryptophan | Dnmtrp | N-(1-methylethyl)glycine | Nval |
| D-N-methyltyrosine | Dnmtyr | N-methyla-naphtylalanine | Nmanap |
| D-N-methylvaline | Dnmval | N-methylpenicillamine | Nmpen |
| γ -aminobutyric acid | Gabu | N-(ρ -hydroxyphenyl)glycine | Nhtyr |
| L-t-butylglycine | Tbug | N-(thiomethyl)glycine | Ncys |
| L-ethylglycine | Etg | penicillamine | Pen |
| L-homophenylalanine | Hphe | L- α -methylalanine | Mala |
| L- α -methylarginine | Marg | L- α -methylasparagine | Masn |
| L- α -methylaspartate | Masp | L- α -methyl-t-butylglycine | Mtbug |
| L- α -methylcysteine | Mcys | L-methylethylglycine | Metg |
| L- α -methylglutamine | Mgln | L- α -methylglutamate | Mglu |
| L- α -methylhistidine | Mhis | L- α -methylhomophenylalanine | Mhphe |
| L- α -methylisoleucine | Mile | N-(2-methylthioethyl)glycine | Nmet |
| L- α -methylleucine | Mleu | L- α -methyllysine | Mlys |
| L- α -methylmethionine | Mmet | L- α -methylnorleucine | Mnle |

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|--|-------|--|--------|
| L- α -methylnorvaline | Mnva | L- α -methylornithine | Morn |
| L- α -methylphenylalanine | Mphe | L- α -methylproline | Mpro |
| L- α -methylserine | Mser | L- α -methylthreonine | Mthr |
| L- α -methyltryptophan | Mtrp | L- α -methyltyrosine | Mtyr |
| L- α -methylvaline | Mval | L-N-methylhomophenylalanine | Nmhphe |
| N-(N-(2,2-diphenylethyl) carbamylmethyl)glycine | Nnbhm | N-(N-(3,3-diphenylpropyl) carbamylmethyl)glycine | Nnbhe |
| 1 -carboxy-1 -(2,2-diphenyl- ethylamino)cyclopropane | Nmbc | | |

23. (Cancelled)

24. (Previously Presented) A method for treatment of inflammation of an airway of an animal, said method comprising administering to said animal, an amount of a peptide effective for treatment of inflammation, said peptide having a sequence comprising SLIGRL (SEQ ID NO:2) or a peptide analog thereof in which an amino acid is replaced with a non-natural amino acid, wherein said peptide is capable of activating an airway epithelium protease activated receptor-2 (PAR2) under conditions sufficient for activation of said PAR2 to occur, thereby providing said treatment of inflammation.

25. (Cancelled)

26. (Previously presented) The method according to Claim 24 wherein the inflammation of the airway is caused by a disease condition selected from the group consisting of asthma, bronchitis, hayfever, alveolitis, ciliary dyskinesis and pulmonary inflammation.

27. (Previously presented)The method according to Claim 24 wherein the peptide comprises the sequence of SEQ ID NO.2.

28. (Previously presented)The method according to Claim 27 wherein the peptide is modified to permit entry across an epithelial and/or subcutaneous layer.

29. (Previously presented)The method according to Claim 27 wherein the peptide is fused to penetratin.

30. (Previously presented) The method according to Claim 27 wherein the peptide is fused to TAT.

31. (Cancelled)

32. (Previously presented) The method of Claim 24, wherein said peptide incorporates a non-natural amino acid listed in the following table:

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|---|-------|-----------------------------|--------|
| α -aminobutyric acid | Abu | L-N-methylalanine | Nmala |
| α -amino- α -methylbutyrate | Mgabu | L-N-methylarginine | Nmarg |
| aminocyclopropane-carboxylate | Cpro | L-N-methyleasparagine | Nmasn |
| aminoisobutyric acid | Aib | L-N-methyleaspartic acid | Nmasp |
| aminonorbornyl-carboxylate | Norb | L-N-methylcysteine | Nmcys |
| cyclohexylalanine | Chexa | L-N-methylglutamine | Nmgln |
| cyclopentylalanine | Cpen | L-N-methylglutamic acid | Nmglu |
| D-alanine | Dal | L-N-methylhistidine | Nmhis |
| D-arginine | Darg | L-N-methylisoleucine | Nmile |
| D-aspartic acid | Dasp | L-N-methylleucine | Nmleu |
| D-cysteine | Dcys | L-N-methyllysine | Nmlys |
| D-glutamine | Dgln | L-N-methylmethionine | Nmmet |
| D-glutamic acid | Dglu | L-N-methylnorleucine | Nmnle |
| D-histidine | Dhis | L-N-methylnorvaline | Nmnva |
| D-isoleucine | Dile | L-N-methylornithine | Nmorn |
| D-leucine | Dleu | L-N-methylphenylalanine | Nmphe |
| D-lysine | Dlys | L-N-methylproline | Nmpro |
| D-methionine | Dmet | L-N-methylserine | Nmser |
| D-ornithine | Dorn | L-N-methylthreonine | Nmthr |
| D-phenylalanine | Dphe | L-N-methyltryptophan | Nmtrp |
| D-proline | Dpro | L-N-methyltyrosine | Nmtyr |
| D-serine | Dser | L-N-methylvaline | Nmval |
| | | L-N-methylethylglycine | Nmetg |
| | | L-N-methyl-t-butylglycine | Nmtbug |

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|----------------------------------|--------|---|--------|
| D-threonine | Dthr | L-norleucine | Nle |
| D-tryptophan | Dtrp | L-norvaline | Nva |
| D-tyrosine | Dtyr | α -methyl-aminoisobutyrate | Maib |
| D-valine | Dval | α -methyl- γ -aminobutyrate | Mgabu |
| D- α -methylalanine | Dmala | α -methylcyclohexylalanine | Mchexa |
| D- α -methylarginine | Dmarg | α -methylcyclopentylalanine | Mcpen |
| D- α -methylasparagine | Dmasn | α -methyl- α -naphthylalanine | Manap |
| D- α -methylaspartate | Dmasp | α -methylpenicillamine | Mpen |
| D- α -methylcysteine | Dmcys | N-(4-aminobutyl)glycine | Nglu |
| D- α -methylglutamine | Dmgln | N-(2-aminoethyl)glycine | Naeg |
| D- α -methylhistidine | Dmhis | N-(3-aminopropyl)glycine | Norn |
| D- α -methylisoleucine | Dmile | N-amino- α -methylbutyrate | Nmaabu |
| D- α -methylleucine | Dmleu | α -naphthylalanine | Anap |
| D- α -methyllysine | Dmlys | N-benzylglycine | Nphe |
| D- α -methylmethionine | Dmmet | N-(2-carbamylethyl)glycine | Ngln |
| D- α -methylornithine | Dmorn | N-(carbamylmethyl)glycine | Nasn |
| D- α -methylphenylalanine | Dmphe | N-(2-carboxyethyl)glycine | Nglu |
| D- α -methylproline | Dmpro | N-(carboxymethyl)glycine | Nasp |
| D- α -methylserine | Dmser | N-cyclobutylglycine | Ncbut |
| D- α -methylthreonine | Dmthr | N-cycloheptylglycine | Nchep |
| D- α -methyltryptophan | Dmtrp | N-cyclohexylglycine | Nchex |
| D- α -methyltyrosine | Dmty | N-cyclodecylglycine | Ncdec |
| D- α -methylvaline | Dmval | N-cyclododecylglycine | Ncdod |
| D-N-methylalanine | Dnmala | N-cyclooctylglycine | Ncoct |
| D-N-methylarginine | Dnmarg | N-cyclopropylglycine | Ncpro |
| D-N-methylasparagine | Dnmasn | N-cycloundecylglycine | Ncund |
| D-N-methylaspartate | Dnmasp | N-(2,2-diphenylethyl)glycine | Nbhm |
| D-N-methylcysteine | Dnmcys | N-(3,3-diphenylpropyl)glycine | Nbhe |

| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|-----------------------------|---------|------------------------------|--------|
| D-N-methylglutamine | Dnmgln | N-(3-guanidinopropyl)glycine | Narg |
| D-N-methylglutamate | Dnmglu | N-(1-hydroxyethyl)glycine | Nthr |
| D-N-methylhistidine | Dnmhis | N-(hydroxyethyl)glycine | Nser |
| D-N-methylisoleucine | Dnmile | N-(imidazolylethyl)glycine | Nhis |
| D-N-methylleucine | Dnmleu | N-(3-indolylethyl)glycine | Nhtrp |
| D-N-methyllysine | Dnmlys | N-methyl-γ-aminobutyrate | Nmgabu |
| N-methylcyclohexylalanine | Nmchexa | D-N-methylmethionine | Dnmmet |
| D-N-methylornithine | Dnmorn | N-methylcyclopentylalanine | Nmcpen |
| N-methylglycine | Nala | D-N-methylphenylalanine | Dnmphe |
| N-methylaminoisobutyrate | Nmaib | D-N-methylproline | Dnmpro |
| N-(1-methylpropyl)glycine | Nile | D-N-methylserine | Dnmser |
| N-(2-methylpropyl)glycine | Nleu | D-N-methylthreonine | Dnmthr |
| D-N-methyltryptophan | Dnmtrp | N-(1-methylethyl)glycine | Nval |
| D-N-methyltyrosine | Dnmtyr | N-methyla-naphtylalanine | Nmanap |
| D-N-methylvaline | Dnmval | N-methylpenicillamine | Nmpen |
| γ-aminobutyric acid | Gabu | N-(p-hydroxyphenyl)glycine | Nhtyr |
| L-t-butylglycine | Tbug | N-(thiomethyl)glycine | Ncys |
| L-ethylglycine | Etg | penicillamine | Pen |
| L-homophenylalanine | Hphe | L-α-methylalanine | Mala |
| L-α-methylarginine | Marg | L-α-methylasparagine | Masn |
| L-α-methylaspartate | Masp | L-α-methyl-t-butylglycine | Mtbug |
| L-α-methylcysteine | Mcys | L-methylethylglycine | Metg |
| L-α-methylglutamine | Mgln | L-α-methylglutamate | Mglu |
| L-α-methylhistidine | Mhis | L-α-methylhomophenylalanine | Mhphe |
| L-α-methylisoleucine | Mile | N-(2-methylthioethyl)glycine | Nmet |
| L-α-methylleucine | Mleu | L-α-methyllysine | Mlys |
| L-α-methylmethionine | Mmet | L-α-methylnorleucine | Mnle |
| L-α-methylinorvaline | Mnva | L-α-methylornithine | Morn |

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| Non-conventional amino acid | Code | Non-conventional amino acid | Code |
|--|-------|--|--------|
| L- α -methylphenylalanine | Mphe | L- α -methylproline | Mpro |
| L- α -methylserine | Mser | L- α -methylthreonine | Mthr |
| L- α -methyltryptophan | Mtrp | L- α -methyltyrosine | Mtyr |
| L- α -methylvaline | Mval | L-N-methylhomophenylalanine | Nmhphe |
| N-(N-(2,2-diphenylethyl) carbamylimethyl)glycine | Nnbhm | N-(N-(3,3-diphenylpropyl) carbamylmethyl)glycine | Nnbhe |
| 1 -carboxy-1 -(2,2-diphenyl- ethylamino)cyclopropane | Nmbc | | |